When is it "Human Subjects Research?" Focus on Social-Behavioral Research

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Presentation Overview

- Applicability of the HHS regulations for the protection of human subjects
- The regulatory definition of *research* and *human subject*
- OHRP Guidance on coded information/specimens
- Exemptions
- Relationship between human subjects research and other activities (e.g., clinical practice, QI/QA activities, oral history activities)
- Examples

Title 45
Code of Federal Regulations
Part 46

Protection of Human Subjects
(Last revised June 23, 2005)

Applicability of the HHS Regulations

- **Research involving human subjects conducted or supported by HHS that is not otherwise exempt**
- **Non-exempt human subjects research conducted at an institution holding an applicable Assurance of Compliance**

Applicability of the HHS Regulations

Research [45 CFR 46.102(d)]?

↓

Human subjects [45 CFR 46.102(f)]?

↓

Exempt [45 CFR 46.101(b)]?

Definition of Research (1)

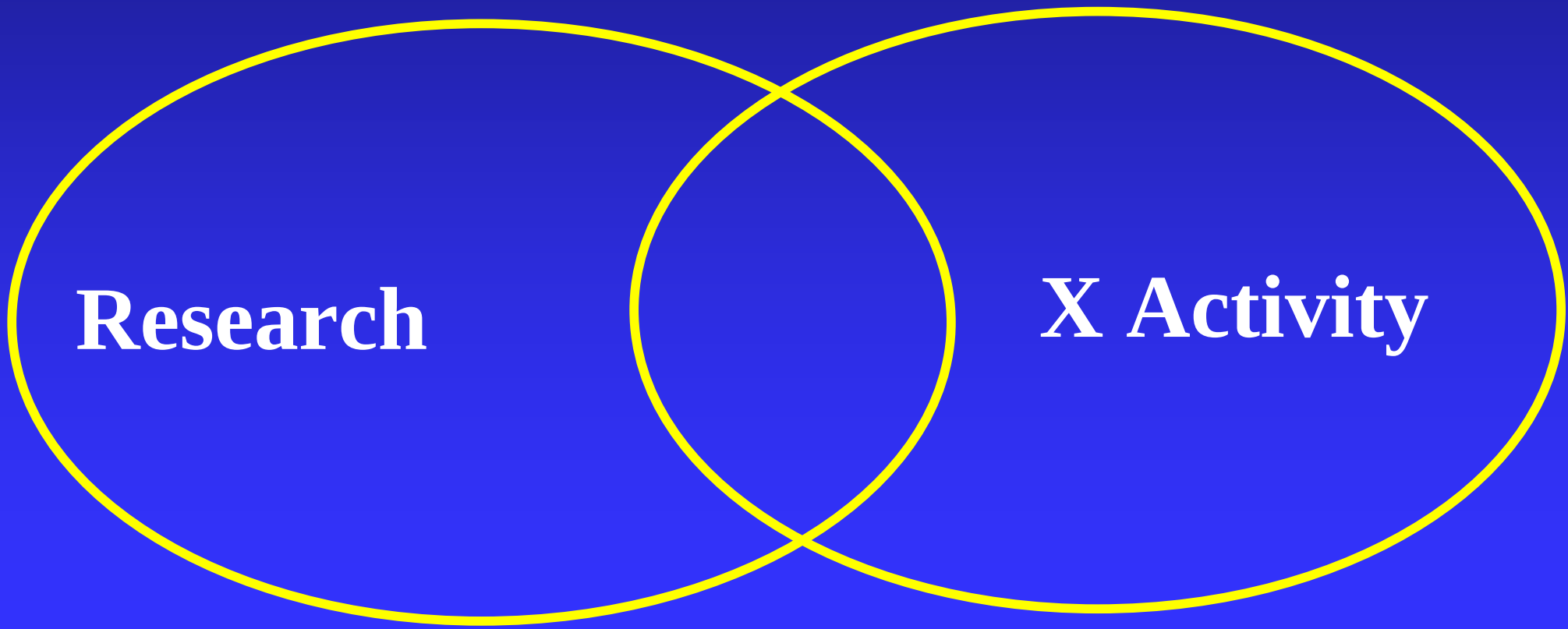
A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. [45 CFR 46.102(d)]

Definition of Research (2)

Activities which meet this definition constitute research for the purposes of [45 CFR part 46] whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities.

[45 CFR 46.102(d)]

Relationship Between Research and Other Types of Activities



Determining Whether an Activity Involves Research

- Does not involve assessment of risks or benefits
- Not defined by any specific type of research design or procedure (e.g., randomization)
- Not dependent upon the testing or evaluation of an “experimental,” “innovative,” or “new” procedure, treatment, or intervention.
- Research may not be primary objective of the activity.
- Publication not definitive feature.

Human Subject

A living individual about whom an investigator conducting research obtains:

(1) Data through intervention or interaction with the individual; or

(2) Identifiable private information.

[45 CFR 46.102(f)]

Identifiable Private Information (1)

Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place.

[45 CFR 46.102(f)]

Identifiable Private Information (2)

Private information includes information which which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). [45 CFR 46.102(f)]

Identifiable Private Information (3)

Private information must be individually identifiable in order for obtaining the information to constitute research involving human subjects. [45 CFR 46.102(f)]

Identifiable Private Information (4)

Individually identifiable: The identity of the subject is or may readily be ascertained by the investigator or associated with the information.

[45 CFR 46.102(f)]

OHRP Guidance on Research Involving Coded Private Information or Biological Specimens (1)

Coded **means that:**

(1) identifying information (such as name or social security number) that would enable the investigator to readily ascertain the identity of the individual to whom the private information or specimens pertain has been replaced with a number, letter, symbol, or combination thereof (i.e., the code); and

(2) a key to decipher the code exists, enabling linkage of the identifying information to the private information or specimens.

OHRP Guidance on Research Involving Coded Private Information or Biological Specimens (2)

- Under the definition of *human subject*, *obtaining* identifiable private information or identifiable specimens for research purposes constitutes human subjects research. *Obtaining* means receiving or accessing identifiable private information or identifiable specimens for research purposes.
- OHRP interprets *obtaining* to include an investigator's use, study, or analysis for research purposes of identifiable private information or identifiable specimens already in the possession of the investigator.

OHRP Guidance on Research Involving Coded Private Information or Biological Specimens (3)

- In general, OHRP considers private information or specimens to be individually identifiable as defined at 45 CFR 46.102(f) when they can be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems.
- Conversely, OHRP considers private information or specimens not to be individually identifiable when they cannot be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems.

OHRP Guidance on Research Involving Coded Private Information or Biological Specimens (4)

For example, OHRP does not consider research involving only coded private information or specimens to involve human subjects as defined under 45 CFR 46.102(f) if the following conditions are both met:

(1) the private information or specimens were not collected specifically for the currently proposed research project through an interaction or intervention with living individuals; and

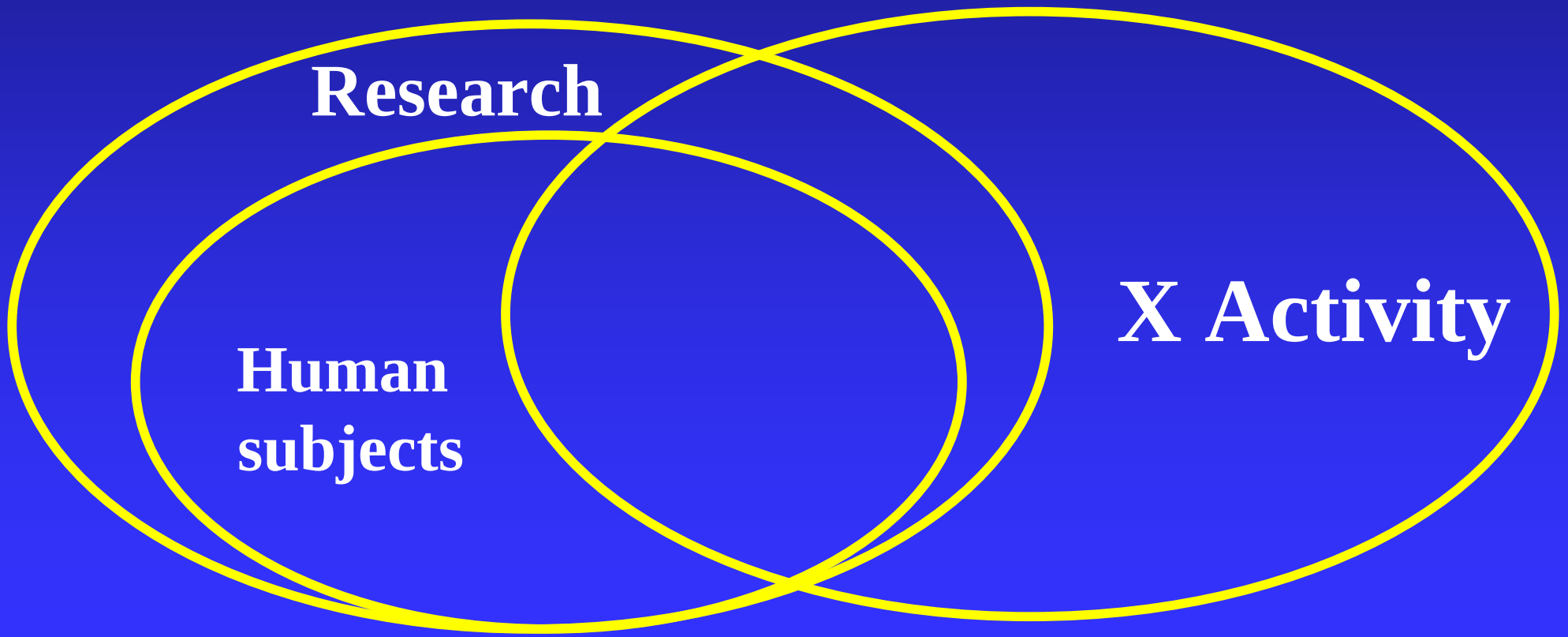
(2) the investigator(s) cannot readily ascertain the identity of the individual(s) to whom the coded private information or specimens pertain because, for example:

…

OHRP Guidance on Research Involving Coded Private Information or Biological Specimens (5)

(a) the key to decipher the code is destroyed before the research begins;
(b) the investigators and the holder of the key enter into an agreement prohibiting the release of the key to the investigators under any circumstances, until the individuals are deceased (note that the HHS regulations do not require the IRB to review and approve this agreement);
(c) there are IRB-approved written policies and operating procedures for a repository or data management center that prohibit the release of the key to the investigators under any circumstances, until the individuals are deceased; or
(d) there are other legal requirements prohibiting the release of the key to the investigators, until the individuals are deceased.

Relationship Between Human Subjects Research and Other Types of Activities



The Belmont Report - Boundary Between Practice and Research (1)

“The distinction between research and practice [X activity] is blurred partly because both often occur together….”

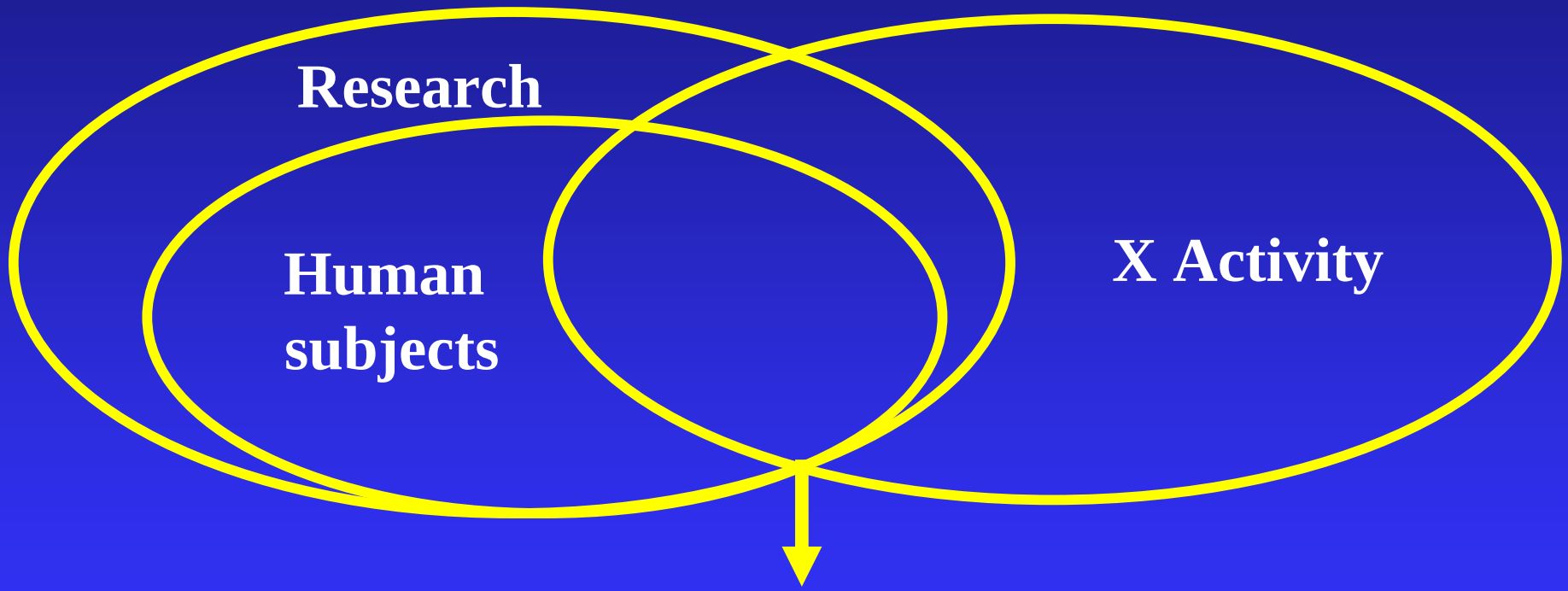
The Belmont Report - Boundary Between Practice and Research (2)

"By contrast, the term 'research' designates an activity designed to test a hypothesis, permit conclusions to be drawn, and thereby develop or contribute to generalizable knowledge…. Research is usually described in a formal protocol that sets forth an objective and a set of procedures designed to reach that objective."

The Belmont Report - Boundary Between Practice and Research (3)

"Research and practice [X activity] may be carried on together when research is designed to evaluate the safety and efficacy of a therapy. This need not cause confusion regarding whether or not the activity requires review; the general rule is that if there is any element of research in an activity, that activity should undergo [IRB] review for the protection of human subjects."

Separating Human Subjects Research from Non-Research Activities



NOTE: In many cases, human subjects research activities can be separated from non-research activities.

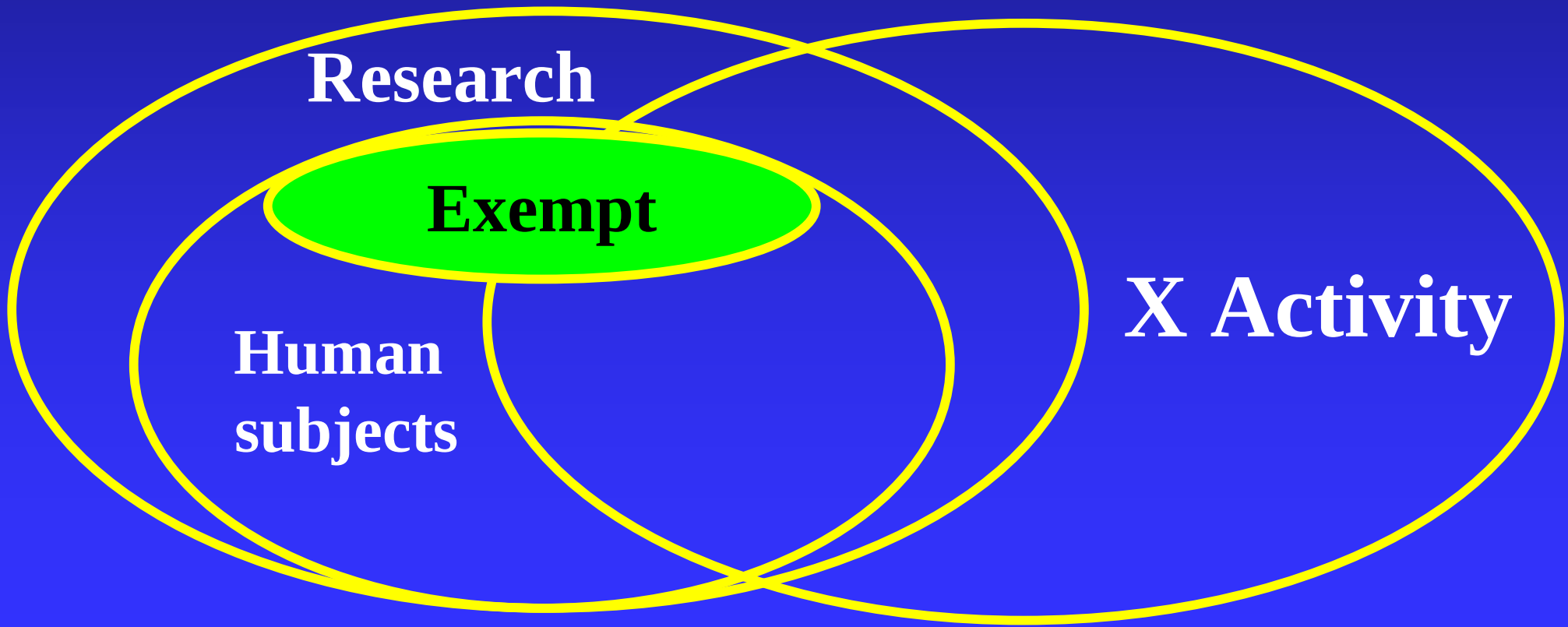
Exemptions (1)

- 45 CFR 46.101(b)(1): Certain research conducted in established or commonly accepted educational settings, involving normal educational practices.
- 45 CFR 46.101(b)(2) and (3): Certain research involving educational tests, survey procedures, interview procedures, or observations of public behavior.

Exemptions (2)

- 45 CFR 46.101(b)(4): Certain research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens.
- 45 CFR 46.101(b)(5): Certain federal research and demonstration projects.
- 45 CFR 46.101(b)(6): Certain taste and food quality evaluation and consumer acceptance studies.

Relationship Between Exempt Human Subjects Research and Non-Research Activities



General Conclusions

- Human subjects research can overlap with other activities.
- Sometimes, human subjects research can be separated from other activities.
- Some of these joint activities are exempt.
- Those that are not exempt must comply with the requirements of 45 CFR part 46 when applicable.

Oral History Activities

Oral History Activities (1)

- Oral history: audio or video-recorded historical information obtained via interviews concerning personal experiences and recollections
- In September 2003, OHRP issued a letter to representatives of oral history societies concurring with the position that oral history activities in general do not represent research as defined at 45 CFR 46.102(d) because not intended to contribute to generalizable knowledge.
- OHRP has not issued guidance on this topic.

Oral History Activities (2)

- A similar position could have been stated for a variety of activities.
- Oral history at times may be research and unless exempt, requires IRB review if HHS regulations apply.
- Some have extrapolated OHRP position to all activities involving qualitative interview procedures.
- Why is oral history on expedited review list?

Oral History Activities (3)

- Non-research examples
  - The oral histories of Holocaust survivors at the U.S. Holocaust Memorial Museum.
  - The oral histories of members and staff of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research available via OHRP website.
- Research example: a study to evaluate the effect of time on memories of traumatic events that involves oral history interviews of subjects at immediately after a traumatic event and one year later.

Quality Assurance/Quality Improvement (QA/QI) Activities

QI/QA Activities (1)

- **Non-research example: peer auditing of healthcare provider medical records with patient-specific and healthcare-provider-specific feedback.**

- **Research example: Fick, DM, et al. A randomized study to decrease the use of potentially inappropriate medications among community dwelling older adults in a southeastern managed care organization. Am J Managed Care. 2004; 10:761-768**

QI/QA Activities (2)

- **Research example:**
  - **Aim: to examine the effectiveness of a strategy to change physician prescribing behavior and decrease use of potentially inappropriate medications (PIM) in members of a managed care organization (MCO).**
  - **Hypothesis: an intervention directed at primary care physicians to decrease PIM will decrease overall number of PIMs prescribed in the intervention group.**
  - **Design: prospective randomized block design**
  - **Study population: all primary care physicians and patients 65 years or older in a MCO. Physicians randomized to usual care or intervention group.**

Am J Manag Care. 2004; 110:761-768

QI/QA Activities (3)

- **Research example (cont):**
  - **Intervention group: (1) personally addressed letter to physician describing in detail all physician's patients who received one or more PIM; (2) detailed education brochure listing PIMs; (3) list of suggested PIM alternative medications (that were independently suggested and reviewed by 5 geriatricians and pharmacists not affiliated with the MCO). Physicians invited to use fax-back form to comment on any PIM prescribing changes in response to (1)-(3).**

Am J Manag Care. 2004; 110:761-768

QI/QA Activities (4)

- **Research example (cont):**
  - **Outcome measures for intervention and control groups: physician behavior change for PIM use, cost and use outcomes, and drug-related problems assessed at 6, 12, and 18 months after the intervention was implemented.**
  - **Conclusion: The intervention was simple and had a decrease in overall PIM prescribing in a sample of older adults. This study describes a low-cost, replicable method to contact and educate physicians on drug therapy issues in older adults.**

Am J Manag Care. 2004; 110:761-768

Documentary Film –
In general, are not research

Research Using Coded Data or Specimens: Does it Involve Human Subjects or is it Exempt Human Subjects Research?

Research With Coded Data (1)

- An investigator receives only coded information on the treatment outcomes of patients treated for arthritis with Drug A versus Drug B from the patients' treating physician. The only involvement of the treating physician is to provide coded information to the investigator. The investigator and the treating physician enter into an agreement prohibiting the release of the key to decipher the code to the investigator under any circumstances, until the individuals are deceased. In this example, the investigator is not conducting human subjects research because the investigator cannot readily ascertain the patients' identity.

Research With Coded Data (2)

- **An investigator obtains individually identifiable information on the treatment outcomes of patients treated for arthritis with either Drug A or Drug B by viewing patients' existing individually identifiable medical records at the clinics where the patients were treated. The investigator records the patients' treatment outcomes in a coded manner that could permit the identification of the patients. In this example, the investigator is conducting human subjects research because the investigator is obtaining identifiable private information from patients' (and now subjects') medical records. The study would not be exempt under 45 CFR 46.101(b)(4) since the investigator is recording the information in a coded manner, thus allowing the subjects to be identified indirectly through identifiers linked to the subjects.**

Research With Coded Data (3)

- An investigator obtains individually identifiable information on the treatment outcomes of patients treated for arthritis with either Drug A or B by viewing existing individually identifiable medical records at the clinics where the patients were treated. The investigator records only patient age, sex, diagnosis, treatment, and health status at the end of 6 months of treatment so that the investigator cannot link the recorded information back to the patients. In this example, the investigator is conducting human subjects research because the investigator is obtaining identifiable private information from patients' (and now subjects') medical records. However, the study would be exempt under 45 CFR 46.101(b)(4).